REMARKS

Claims 1, 3, 5-21, 23, 25-27, 40 and 44 are pending in the above-identified application. The proviso at the end of claim 1 has been deleted. Also, claims 1, 14, 15, 23 and 26 have been amended to delete some portions of variable definitions, as well as some specifically listed compounds, so as to further define these claims over the cited references. Claim 13 has been amended to correct an inadvertent omission in that "alkoxycarbamoyl" has been inserted as fully supported at page 5, lines 13-14 of the specification.

Information Disclosure Statement Will Be Filed

Applicant will submit an Information Disclosure Statement (IDS) supplemental to this Amendment in the near future, likely within the next few weeks. It is requested that the Examiner await receipt of this IDS before acting on this application.

Unity of Invention Requirement

Applicant's traversal of the Unity of Invention Requirement in the Response filed November 16, 2009 is maintained for the reasons stated which are deemed repeated herein.

Issues under 35 USC 112, second paragraph

Claims 1, 3, 5-21, 23, 25 and 27 have been rejected under 35 USC 112, second paragraph, as allegedly being indefinite because of the proviso previously recited at the end of claim 1. Claim 1 has been amended to remove the proviso, as well as to delete portions of some variable definitions, such that the basis for this rejection has been removed and the rejection should be withdrawn.

Issues under 35 USC 102(b) and 103(a)

Claims 1, 3, 5-6, 8, 10-11, 13-21, 23 and 25-26 have been rejected under 35 USC 102(b) as being anticipated by Beilstein Registry, (XP-002319951, XP-002319952 and XP-002319954).

Claims 1, 3, 5-21, 23 and 25-27 have been rejected under 35 USC 103(a) as being unpatentable over Beilstein Registry (XP-002319951), Bridges '235 (WO 00/40235), Barrett '426 (WO 99/01426), Barrett '191 (WO 03/62191), Barrett '213 (WO 02/06213), Barrett '189 (WO

03/62189), Dudley '436 (WO 00/35436) and individually in view of King (Med. Chem: Principle and Practice (1994), p. 206-208).

These rejections are traversed based on the reasons below.

Removal of Basis for Rejections under 35 USC 102(b)

The basis for the above rejections under 35 USC 102(b) over Beilstein Registry has been removed, since the deletion from the substituent "X" definition of "$-(CH_2)_k$-C(O)-$(CH_2)_m$-" removes potential compounds based on XP-002319951 and XP-002319954, while the deletion of "$-(CH_2)_w$-C(O)-NH-$(CH_2)_z$-" removes potential compounds based on XP-002319952. Thus, it is requested that this rejection be withdrawn.

Distinctions over References Cited under 35 USC 103(a)

As noted above, the changes to claim 1 have removed any potential compounds based on Beilstein Registry XP-002319951 (7/11/89). Beilstein XP '951 is focused on synthesis methods. At page 6282 it is stated that, "...limited pharmacological examination revealed no activity of interest." Consequently, one skilled in the art would not have had a reasonable basis to attempt to modify the structure of the disclosed compounds in an attempt to arrive at the presently claimed compounds, because there would not have been a reasonable expectation of success in doing so.

It is further submitted that common to all of the cited Bridges '235, Barrett '426, Barrett '191, Barrett '213, Barrett '189, Dudley '436 and King references is the fact that all of the disclosed compound structures require that the substituent corresponding to "X" in the present claims must be a bond. However, X cannot be a bond as recited in the present claims. Applicant submits that a person skilled in the art would not be motivated to modify the diphenylamine skeleton essential for MEK inhibitors by inserting a linking group X (as defined in the present claims) between the phenyl ring and the amino group of the compounds disclosed in these references. In fact, the diphenylamine skeleton forms an essential and mandatory part of the structure in the compounds disclosed by these references. There are absolutely no hints or suggestions in any of these cited references alone or in combination with King, that inserting a linking group X into this essential part of the structure skeleton would provide suitable KDR-inhibitory compounds with an *in vitro* KDR-inhibitory activity as listed for the compounds claimed in the present invention and noted at pages 306-310 of the published PCT version. The

cited references disclose compounds which are MEK inhibitors and are silent about any KDR inhibitory activity. It would therefore have not been obvious for one skilled in the art to predict that the X-linker-2-amino substituted benzohydroxamic esters of the present invention would affect KDR inhibitory activity as exhibited by the compounds of the present invention.

The Examiner attempts to rely on *In re Henze*, 85 USPQ 261 (1950) for the proposition that the burden is on Applicant to show that the claimed compounds possesses unobvious beneficial properties not actually possessed by a prior art homolog. The Examiner also characterizes the presently claimed compounds as being adjacent homologs (if X is alkylene) of prior art compounds (X is a bond). However, *Henze* cannot be relied upon, since the presently claimed compounds do not correspond to the "homologs" addressed in *Henze*. In *Henze*, the homologs in question were compounds differing by the replacement of a terminal ethyl with a terminal isopropyl. The compounds of the cited references above do not differ by substitution of a terminal alkyl group, but rather differ from replacement of a bond with an alkylene or other significant linking group. One simply cannot characterize the presently claimed compounds as being "adjacent homologs" of the compounds in the cited references. For example, an essential phenyl-N-phenyl portion of a disclosed compound from the cited references cannot be characterized as a "homolog" of a phenyl-N-X-phenyl portion of the compounds of the present invention with "X" being a linker group, not a bond.

In addition, it is noted that the Examiner has referred to King. However the cited pages of King do not suggest the replacement of a "bond" with any of the linking groups included in the definition of "X" in claim 1. Also, King fails to suggest any replacement of —NH— with —N-alkyl— or any other —N-X— group as recited in the present claims.

In order to further support the advantageous properties of the compounds of the present invention, it is noted that in Table 6 at page 313 of the specification, the results of tests conducted by Applicant show that the claimed compounds exhibit unexpected beneficial properties not possessed by similar compounds of the prior art (WO 00/027819). The data in Table 6 of the present specification clearly indicate that the compounds claimed in the present invention possess an unobvious beneficial property (increased metabolic stability) compared to prior art compounds, where a bivalent —O— group has been inserted in place of an isosteric bivalent —CH_2— group.

In conclusion, it is submitted that the compounds of the present invention are patentable and non-obvious over compounds disclosed by the above cited references since a person skilled in the art would not have been motivated to make ortho-amino substituted (hetero)aromatic hydroxamic esters, wherein the substituent to the ortho-amino group is linked via a linker group X, that is not a bond, since there was no basis for any reasonable expectation that such compounds would be KDR inhibitors. Consequently, the above rejections must be withdrawn.

If any questions arise in the above matters, please contact Applicant's representative, Andrew D. Meikle (Reg. No. 32,868), in the Washington Metropolitan Area at the phone number listed below.

If necessary, the Director is hereby authorized in this, concurrent, and future replies to charge any fees required during the pendency of the above-identified application or credit any overpayment to Deposit Account No. 02-2448.

Dated: July 26, 2010

(Monday)

Respectfully submitted,

By_____
Andrew D. Meikle
Registration No.: 32868
BIRCH, STEWART, KOLASCH & BIRCH, LLP
8110 Gatehouse Road, Suite 100 East
P.O. Box 747
Falls Church, VA 22040-0747
703-205-8000